Amendments to the Claims – Marked Up Version

Claims 1, 2, 7 and 8 are currently under prosecution. Claims 3-6 and 9-17 are withdrawn to non-elected matter.
Claims 1, 2, 7 and 8 are currently amended.

1. (Currently Amended) A method for identifying an agent which modulates the binding of a **Repulsive Guidance Molecule** (RGM) to a Neogenin, the method comprising the steps of: (a) forming a mixture comprising an isolated mammalian RGM and an isolated mammalian Neogenin; (b) incubating said mixture in the presence of an agent; and (c) detecting in the incubated mixture of step (b) the level of specific binding between said RGM and said Neogenin, wherein a difference in the detected level of specific binding of said RGM to said Neogenin in the presence of said agent relative to the level of specific binding in the absence of said agent indicates that said agent modulates the binding of said RGM to said Neogenin.

2. (Currently Amended) A method for monitoring the ~~interaction~~ binding ~~between~~ of ~~an~~ **Repulsive Guidance Molecule** (RGM) ~~and~~ **to** a Neogenin, the method comprising the steps of: (a) contacting a first protein comprising the RGM **tagged with a visible stain or enzymatic signal,** with a second protein which comprises the Neogenin, **and with a RGM-specific antibody or small molecule which will interfere in the binding between the tagged RGM and the Neogenin; (b) leaving the mixture for a time and** under conditions where a domain of the RGM binds to a domain of the Neogenin; (~~c~~**b**) **monitoring the** ~~determining~~ the binding of the first protein **which comprises the tagged RGM,** to the second protein **which comprises the Neogenin, wherein a reduction in the visible stain or enzymatic signal indicates a reduction** ~~or second protein to the first protein~~ **of tagged RGM binding to Neogenin due to the antibody or small molecule interacting with said binding.**~~.~~

3. (Withdrawn) A method for monitoring the interaction between a RGM and a Neogenin, the method comprising the steps of: (a) contacting a fusion protein comprising

an RGM domain with cells which express a Neogenin; (b) detecting the fusion protein comprising the RGM domain which binds to the cells.

4. (Withdrawn) A method for monitoring the interaction between a RGM and a Neogenin, the method comprising the steps of: (a) contacting a protein comprising a RGM domain with cells which express a polypeptide comprising the Neogenin; (b) detecting the protein comprising the RGM domain which binds to the cells.

5. (Withdrawn) A method for monitoring the interaction between a RGM and a Neogenin, the method comprises the steps of: (a) co-culturing in a matrix (a) embryonic nerve cells with (b) cells which have been transfected with an expression construct encoding the RGM and which express the Neogenin; (b) adding to the cells an inhibitor of binding of the RGM and Neogenin; (c) determining the axon outgrowth adjacent to the cells which express the RGM in the presence and absence of inhibitor.

6. (Withdrawn) A method for monitoring the interaction between a RGM and a Neogenin, the method comprising the steps of: (a) culturing embryonic nerve cells under conditions in which they display growth cones; (b) contacting the embryonic nerve cells with the RGM and an anti-Neogenin antibody; (c) observing the effect of the antibody on the collapse of the growth cones.

7. (Currently Amended) A method according to any one of claims 1-~~6~~2, wherein said RGM is a human RGM.

8. (Currently Amended) A method according to any one of claims 1-~~6~~2, wherein said Neogenin is a human Neogenin.

9. (Withdrawn) A mixture comprising an isolated mammalian RGM and an isolated mammalian Neogenin.

10. (Withdrawn) A mixture according to claim 9, wherein said RGM is a human RGM or

said Neogenin is human Neogenin.

11. (Withdrawn) A mixture according to claim 9, wherein said RGM is a human RGM and said Neogenin is human Neogenin.

12. (Withdrawn) A method of enhancing axon outgrowth comprising inhibiting the interaction between RGM and Neogenin.

13. (Withdrawn) A polypeptide portion of Neogenin useful for antagonizing the interaction between RGM and Neogenin.

14. (Withdrawn) An antibody preparation which specifically inhibits the interaction of a Neogenin protein and an RGM protein.

15. (Withdrawn) A use of an inhibitor capable of modulating the interaction between RGM and Neogenin in the prevention or treatment of a disease or condition associated with the degeneration or injury of vertebrate nervous tissue.

16. (Withdrawn) The use of claim 15 wherein said diseases or conditions associated with the degeneration or injury of vertebrate nervous tissue are selected from the group consisting of neurodegenerative diseases, nerve fiber injuries and disorders related to nerve fiber losses.

17. (Withdrawn) The use of claim 16, wherein said neurodegenerative disease is selected from the group consisting of motorneuronal diseases (MND), ALS, Alzheimer disease, Parkinsons disease, progressive bulbar palsy, progressive muscular atrophy, HIV-related dementia and spinal muscular atrophy(ies), Down's Syndrome, Huntington's Disease, Creutzfeldt-Jacob Disease, Gerstmann-Straeussler Syndrome, kuru, Scrapie, transmissible mink encephalopathy, other unknown prion diseases, multiple system atrophy, Riley-Day familial dysautonomia wherein said nerve fiber injuries are selected from the group consisting of spinal cord injury(ies), brain injuries related to raised

intracranial pressure, trauma, secondary damage due to increased intracranial pressure, infection, infarction, exposure to toxic agents, malignancy and paraneoplastic syndromes and wherein said disorders related to nerve fiber losses are selected from the group consisting of paresis of nervus facials, nervus medianus, nervus ulnaris, nervus axillaris, nervus thoracicus longus, nervus radialis and for of other peripheral nerves.

Remarks

Sequence Compliance

The Office Action states that the present application fails to comply with the requirements of 37 C.F.R §1.821 – §1.825. Applicants respectfully disagree. The present U.S. patent application publication US2006/0252101 presents the required reference to the relevant sequences in page 14 to page 20, under the title "SEQUENCE LISTING".

Drawings

Figures 5, 6A and 6B are objected because are included in the specification, which is not permitted according to 37 C.F.R §1.83(a) and §1.58(a). Applicants respectfully submit that the present application was accepted for national patentability examination in the United States Patent and Trademark Office after meeting the requirements under 35 U.S.C. § 371 of PCT/US03/20147. Accordingly. The present application was filed under 35 U.S.C. § 371, and therefore is exempt from 37 C.F.R §1.83(a) and §1.58(a).

Figures

A new set of figures is included with the present reply. If the Examiner considered that the quality is not good enough, electronic copies and original photographs are available.

Claim Objection

Claims 1 and 2 are objected for informalities. Applicants have amended claims 1 and 2 by reciting the meaning of "RGM". Applicants have also amended claims 7 and 8 to indicate proper dependency.

Claim Rejection under 35 U.S.C. § 112, second paragraph.

Claims 1, 7, and 8 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. Applicants respectfully disagree with the Examiner's statement. The term "modulation" is defined in the specification as being preferably an "inhibition" ([0077], page 5 of US2006/0252101). To apprise the skilled in the art of the scope of the invention, the term "modulator" is also defined as being

preferably an "inhibitor"([0085] page 6, and [0108] page 8 of US2006/0252101). Accordingly, Applicants submit that the specification provides the required guidance to the skilled in the art as to the scope of claim 1, 7 and 8.

The Office Action states that Claim 2 is unclear as to the term "monitoring". Applicants have amended claim 2 to make more clear that the monitoring implies determining the binding of the RGM protein to the Neogenin protein, and how much the binding is affected by agents, such as antibodies or small compounds.

The Office Action states that Claims 1 and 2 are unclear because "a Neogenin" is interpreted as "any Neogenin" which may include "splice variants, etc". Applicants would like to draw the Examiner's attention to [0082] of US2006/0252101, in which it is clearly described what is intended by a Neogenin, i.e. homologues and variants. The skilled in the art is aware that human Neogenin exists in two different splice forms with Neogenin products of 1461 and 1408 amino acids, these two isoforms differ by a 159 base pair fragment in the cytoplasmic domain (Meyerhardt et al., Oncogene Vol. 14 pages 1129-1136, 1997). Because these variants are not different in their extracellular RGM binding domain, alternative splicing does not influence the binding to RGMs. Neogenin.

Claim Rejection under 35 U.S.C. § 112, first paragraph.

Claims 1, 2, 7 and 8 are rejected under 35 U.S.C. § 112, first paragraph, as not being enabled for the binding of any RGM to Neogenin. Applicants submit that the specification describes the binding of chick RGM, mouse RGM-A and mouse RGM-B all bind to Neogenin (See Figure 1, and paragraph [0070]). For the purpose of clarification, RGM A is the most closely related RGM orthologue of chick RGM, it is localized in chromosome 15q26.1 and is also referred as to RGM 15. RGM B is localized in chromosome 5q21.1 and is also referred as to RGM 5, and RGM C is localized in chromosome 1q21.1, therein the reference to RGM 1. Therefore, Applicants submit that with the information provided in the specification allows one skilled in the art enough guidance to identify an agent that will modulate the binding of these molecules with a reasonable amount of success without undue experimentation.

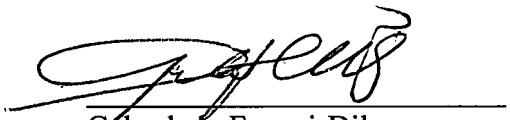
Conclusion

Applicants respectfully submit that all objections and rejections have been adequately addressed. In view of the amendments and the aforementioned remarks, Applicants respectfully believe that the application is now in condition for allowance and respectfully request that the Examiner to withdraw all outstanding rejections and to pass this application to allowance.

Respectfully submitted,
Stephen Strittmatter, et al.

23492

ABBOTT LABORATORIES
D-0377/AP6A-1
100 Abbott Park Road
Abbott Park, IL 60064-6008
Tel No.: (847) 935-4314
Fax No.: (847) 938-2623



Gabryleda Ferrari-Dileo
Registration No. 55,174
Attorney for Applicant(s)